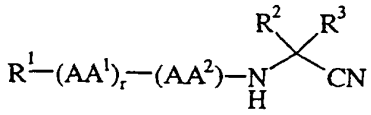
CLAIMS

1. A compound of formula (I):



(I)

wherein

r is 0 or 1;

$\mathbf{R^1}$ is hydrogen, optionally substituted benzyl where said optional substituents are chosen from one or more of C_{1-6}alkyl, halo, trifluoromethyl, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, C_{1-6}alkylamino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, nitro, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, mercapto, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)sulphamoyl and *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl, or R^1 is a group of formula (II):

(II)

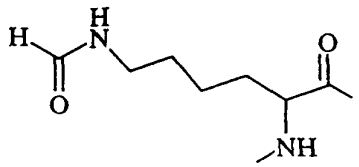
wherein $\mathbf{R^5}$ is C_{1-6}alkyl (optionally substituted with an optionally substituted phenyl, an optionally substituted 5 or 6 membered heteroaryl ring, optionally substituted phenoxy, optionally substituted phenylsulphonyl, optionally substituted C_{3-12}cycloalkyl or Het), C_{1-6}alkoxy, optionally substituted phenyl, optionally substituted naphthyl, optionally substituted 5 or 6 membered heteroaryl ring, optionally substituted C_{3-12}cycloalkyl, Het or optionally substituted phenylC_{1-6}alkoxy; where said optional substituents are chosen from one or more of C_{1-6}alkyl, halo, trifluoromethyl, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, C_{1-6}alkylamino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, nitro, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, mercapto,

C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)sulphamoyl and *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl;

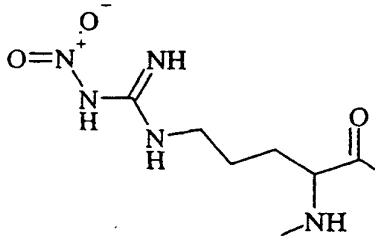
$\mathbf{R^2}$ is H, C_{1-6}alkyl [optionally substituted with one or more of hydroxy, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, R^4, R^4C_{1-6}alkylsulphanyl, R^4C_{1-6}alkylsulphinyl, R^4C_{1-6}alkylsulphonyl], or R^2 is C_{1-6}alkoxy [optionally substituted with one or more of C_{2-6}alkenyl, C_{2-6}alkynyl, R^4, R^4C_{2-6}alkenyl, R^4C_{2-6}alkynyl, Het and trifluoromethyl], or R^2 is C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxycarbonyl, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, R^4, R^4S, R^4C_{1-6}alkylsulphanyl, *N*-(R^4C_{1-6}alkyl)carbamoyl, *N*-(HetC_{1-6}alkyl)carbamoyl, C_{1-6}alkanoylamino, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl or C_{1-6}alkylsulphonyl; $\mathbf{R^4}$ is an optionally substituted phenyl or an optionally substituted 5 or 6 membered heteroaryl ring containing a maximum of four heteroatoms, said optional substituents being chosen from one or more of C_{1-6}alkyl, halo, trifluoromethyl, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, C_{1-6}alkylamino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, nitro, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, mercapto, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)sulphamoyl and *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl;

$\mathbf{R^3}$ is H or C_{1-6}alkyl;

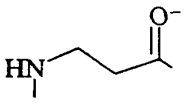
($\mathbf{AA^1}$) and ($\mathbf{AA^2}$) are independently chosen from Ala, Arg, Cys, Gly, His, Ile, Leu, Lys, Met, Phe, Ser, Thr, Trp, Tyr, Val,



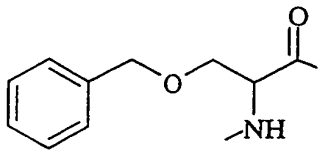
Lys(CHO),



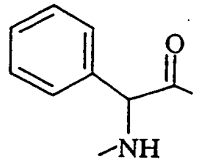
Arg(NO_2),



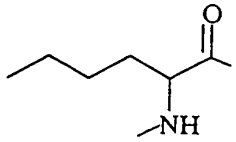
β-Ala,



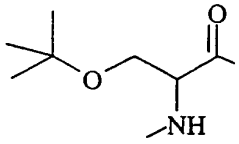
Ser(Bzl),



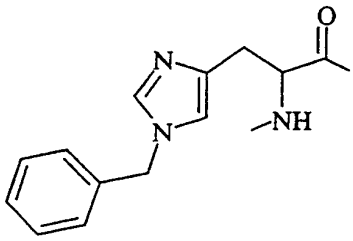
Ph-Gly,



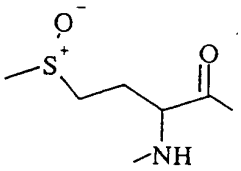
Nle,



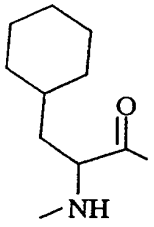
Ser(O^{t}Bu),



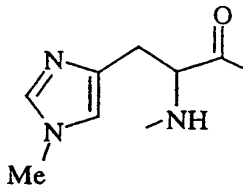
His(Bzl),



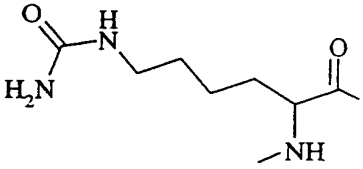
Met(O),



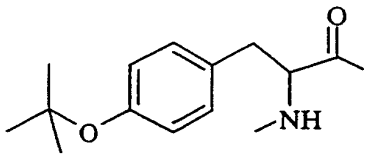
Cha,



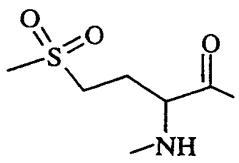
His(Me),



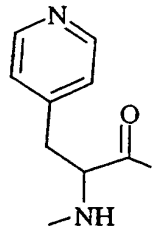
Cit,



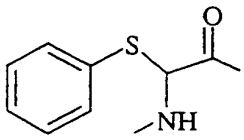
Tyr(^{t}Bu),



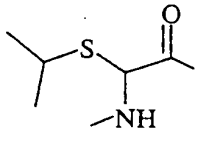
Met(O_2),



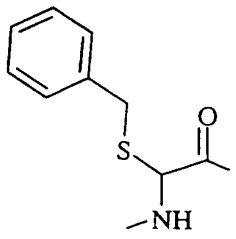
Pyr-Ala



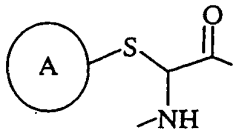
Phe(S),



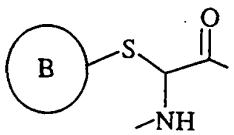
Leu(S),



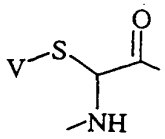
Phe(CH_2S),



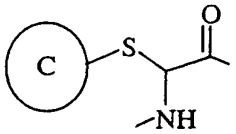
Cy(S)-Gly,



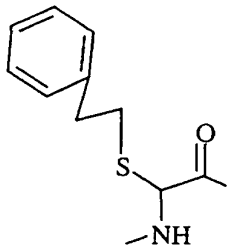
Hetar(S)-Gly,



alk(S)-Gly or



Het(S)-Gly, and



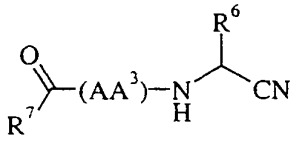
Phe(CH_2CH_2)S;

wherein Ring A is C_{3-12}cycloalkyl; Ring B is a 5 or 6 membered heteroaryl ring; Ring C is Het; V is C_{1-6}alkyl excluding isopropyl; the nitrogen of the amino acid may optionally be alkylated with C_{1-6}alkyl; the phenyl group of Phe(S) and Rings A and B are optionally substituted with one or more of C_{1-6}alkyl, halo, trifluoromethyl, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, C_{1-6}alkylamino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, nitro, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, mercapto, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)sulphamoyl or *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl; the phenyl group of Phe(S) may be fused to another phenyl group to form a naphthyl group; the sulphur moiety in the ∝-position of the amino acid (AA^3) may be optionally oxidised to form an -$S(O)_2$- or -S(O)- moiety; and

Het is a fully saturated monocyclic 5 - 8 membered heterocyclic ring, with up to 4 ring heteroatoms;

or a pharmaceutically acceptable salt thereof.

2. A compound as claimed in claim 1 having the formula (**Ia**):



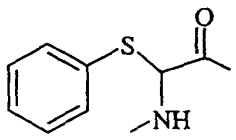
(Ia)

wherein:

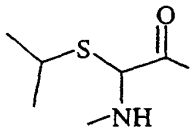
$\mathbf{R^7}$ is optionally substituted benzyl, optionally substituted phenoxymethyl, optionally substituted phenylsulphonylmethyl, optionally substituted benzyloxy, optionally substituted naphthyl, optionally substituted phenyl or t-butoxy where said optional substituents are chosen from one or more of C_{1-6}alkyl, halo, trifluoromethyl, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, C_{1-6}alkylamino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, nitro, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, mercapto, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)sulphamoyl and *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl;

$\mathbf{R^6}$ is hydrogen, optionally substituted phenyl or optionally substituted 5 or 6 membered heteroaryl ring containing a maximum of four heteroatoms; said optional substituents being chosen from one or more of C_{1-6}alkyl, halo, trifluoromethyl, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, C_{1-6}alkylamino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, nitro, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, mercapto, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)sulphamoyl and *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl;

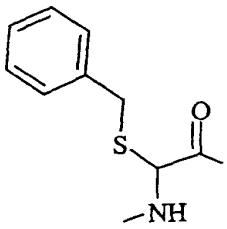
($\mathbf{AA^3}$) is selected from:



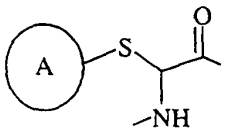
Phe(S),



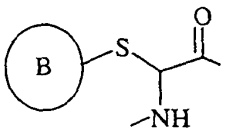
Leu(S),



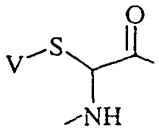
Phe(CH_2S),



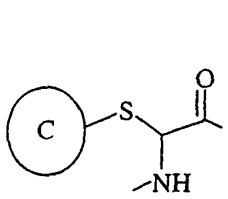
Cy(S)-Gly,

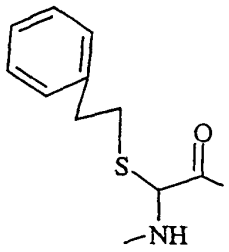


Hetar(S)-Gly,



alk(S)-Gly and





Het(S)-Gly, and Phe(CH_2CH_2)S;

wherein Ring A is C_{3-12}cycloalkyl, Ring B is a 5 or 6 membered heteroaryl ring, Ring C is Het, V is C_{1-6}alkyl excluding isopropyl; the nitrogen of the amino acid may optionally be alkylated with C_{1-6}alkyl; the phenyl group of Phe(S) and Rings A and B may be optionally substituted with one or more of C_{1-6}alkyl, halo, trifluoromethyl, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, C_{1-6}alkylamino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, nitro, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, mercapto, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)sulphamoyl and *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl; the phenyl group of Phe(S) may be fused to another phenyl group to form a naphthyl group; the sulphur moiety in the ∝-position of the amino acid (AA^3) may be optionally oxidised to form an -$S(O)_2$- or -S(O)- moiety; and

Het is a fully saturated monocyclic 5 - 8 membered heterocyclic ring, with up to 4 ring heteroatoms;

or a pharmaceutically acceptable salt thereof.

3. A compound as claimed in claim 2 wherein R^6 is hydrogen, optionally substituted phenyl or a 5 membered heteroaryl ring containing a maximum of four heteroatoms.

4. A compound as claimed in claim 2 or 3 wherein R^7 is benzyl (optionally substituted with halo (such as chloro)), α-(C_{1-4} alkyl)-benzyl (optionally substituted with halo (such as chloro)), α,α-di(C_{1-4} alkyl)-benzyl (optionally substituted with halo (such as chloro)), optionally substituted phenoxymethyl, phenylsulphonylmethyl, benzyloxy, naphthyl or optionally substituted phenyl where said optional substituents are chosen from one or more halo.

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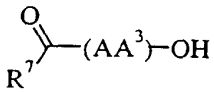
5. A compound as claimed in claim 2, 3 or 4 wherein (AA^3) is Leu(S), Phe(S) optionally substituted with C_{1-6}alkyl or halo and wherein the phenyl group of Phe(S) may be fused to another phenyl group to form a naphthyl group or the sulphur moiety in the ∝-position of the amino acid (AA) may be optionally oxidised to form an $-S(O)_2-$ or Phe(CH_2S).

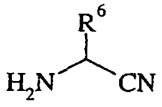
6. A process for preparing a compound of formula (Ia) as claimed in claim 2 comprising:

a) coupling an acid of formula **(IIIa)**:



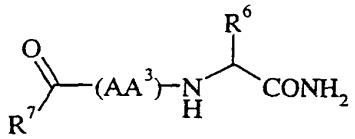
(IIIa)

or a reactive derivative thereof, with an amine of formula **(IVa)**:



(IVa)

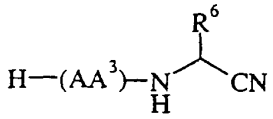
b) dehydrating a compound of formula **(Va)**:



(Va)

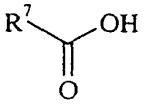
under standard conditions; or,

c) reacting an amine of formula **(VIa)**:



(VIa)

with an acid of formula **(VIIa)**:

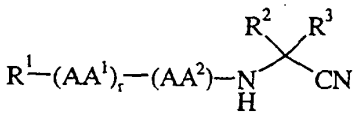


(VIIa)

or a reactive derivative thereof;

wherein R^6, R^7 and AA^3 are as defined in claim 2.

7. A compound of formula (I):



(I)

wherein:

r is 0 or 1;

R^1 is optionally substituted benzyl where said optional substituents are chosen from one or more of C_{1-6}alkyl, halo, trifluoromethyl, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, C_{1-6}alkylamino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, nitro, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, mercapto, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)sulphamoyl and *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl or R^1 is a group of formula (II):

(II)

wherein R^5 is C_{1-6}alkyl (optionally substituted with an optionally substituted phenyl, an optionally substituted 5 or 6 membered heteroaryl ring, optionally substituted phenoxy or optionally substituted phenylsulphonyl), C_{1-6}alkoxy, optionally substituted phenyl, optionally substituted naphthyl, optionally substituted phenylC_{1-6}alkoxy where said optional substituents are chosen from one or more of C_{1-6}alkyl, halo, trifluoromethyl, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, C_{1-6}alkylamino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, nitro, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, mercapto, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl,

C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)sulphamoyl and *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl;

R^2 is H, C_{1-6}alkyl [optionally substituted with one or more of hydroxy, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, R^4, R^4C_{1-6}alkylsulphanyl, R^4C_{1-6}alkylsulphinyl, R^4C_{1-6}alkylsulphonyl], or R^2 is C_{1-6}alkoxy [optionally substituted with one or more of C_{2-6}alkenyl, C_{2-6}alkynyl, R^4, R^4C_{2-6}alkenyl, R^4C_{2-6}alkynyl, Het and trifluoromethyl], or R^2 is C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxycarbonyl, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, R^4, R^4S, R^4C_{1-6}alkylsulphanyl, *N*-(R^4C_{1-6}alkyl)carbamoyl, *N*-(HetC_{1-6}alkyl)carbamoyl, C_{1-6}alkanoylamino, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl wherein **R^4** is an optionally substituted phenyl, or an optionally substituted 5 or 6 membered heteroaryl ring containing a maximum of four heteroatoms said optional substituents being chosen from one or more of C_{1-6}alkyl, halo, trifluoromethyl, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, C_{1-6}alkylamino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, nitro, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, mercapto, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)sulphamoyl and *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl;

R^3 is H or C_{1-6}alkyl; and

(**AA^1**) and (**AA^2**) are independently chosen from Ala, Arg, Cys, Gly, His, Ile, Leu, Lys, Met, Phe, Ser, Thr, Trp, Tyr, Val, Lys(CHO), Arg(NO_2), β-Ala, Ser(Bzl), Ph-Gly, Nle, Ser(O^{t}Bu), His(Bzl), Met(O), Cha, His(Me), Cit, Tyr(^{t}Bu), Met(O_2), Pyr-Ala, Phe(S), Leu(S) or Phe(CH_2S); wherein the nitrogen of the amino acid may optionally be alkylated with C_{1-6}alkyl and the phenyl group of Phe(S) may be optionally substituted with one or more of C_{1-6}alkyl, halo, trifluoromethyl, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, C_{1-6}alkylamino, *N,N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, nitro, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, mercapto, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)sulphamoyl and *N,N*-(C_{1-6}alkyl)$_2$sulphamoyl or the phenyl group may be fused to another phenyl group to form a naphthyl group; or a pharmaceutically acceptable salt thereof.

8. A compound of formula (I) as claimed in claim 7 wherein r is 0; and R^2 is furyl, pyrazolyl (optionally substituted with one or more of methyl and bromo), imidazolyl, 1,2,4-triazolyl, benzyl, 2-methylthioethyl, isopropylthio, methoxy, isopropoxy and 2-propynyloxy.

9. A compound of formula (I) as claimed in claim 1 wherein r is 0; and R^2 is thienyl.

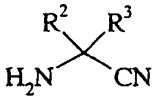
10. A process for preparing a compound of formula (I) as claimed in claim 1 comprising:

a) coupling an acid of formula (**III**):

$$R^1-(AA^1)_r-(AA^2)-OH$$

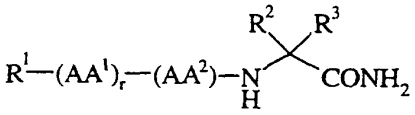
(**III**)

or a reactive derivative thereof, with an amine of formula (**IV**):



(**IV**)

b) dehydrating a compound of formula (**V**):



(**V**)

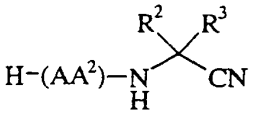
under standard conditions;

c) for compounds of formula (**I**) where r = 1, coupling an acid of formula (**VI**):

$$R^1-(AA^1)-OH$$

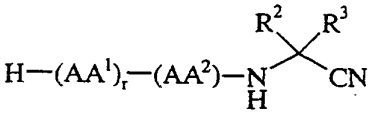
(**VI**)

or a reactive derivative thereof as defined hereinbefore, with an amine of formula (**VII**):



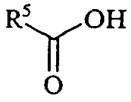
(**VII**)

d) for compounds of formula (I) where R^1 is a group of formula (II), reacting an amine of formula (VIII):



(VIII)

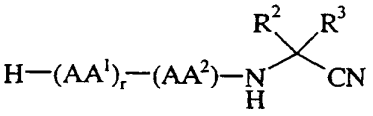
with an acid of formula (IX):



(IX)

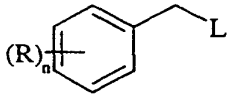
or a reactive derivative thereof as defined hereinbefore; or

e) for compounds of formula (I) where R^1 is optionally substituted benzyl, reacting an amine of formula (X):



(X)

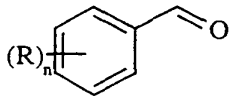
i) with a compound of formula (XI):



(XI)

where $(R)_n$ are optional substituents as defined above and L is a displaceable group; or

ii) with an aldehyde of formula (XII):

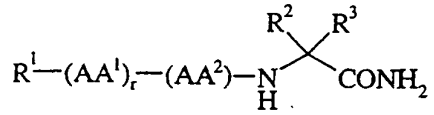


(XII)

where $(R)_n$ are optional substituents as defined above and L is a displaceable group;

wherein R^1, R^2, R^3, AA^1, AA^2 and r are as defined in claim 1.

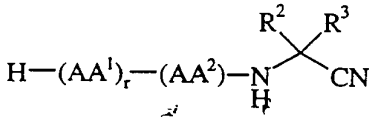
11. A compound of formula (V):



(V)

wherein R^1, R^2, R^3, AA^1, AA^2 and r are as defined in claim 1.

12. A compound of formula (VIII):



(VIII)

wherein R^1, R^2, R^3, AA^1, AA^2 and r are as defined in claim 1.

13. A pharmaceutical composition comprising a compound of formula (I) or (Ia), or a pharmaceutically acceptable salt thereof, as claimed in claim 1, 2, 8 or 9 and a pharmaceutically acceptable diluent or carrier.

14. A compound of formula (I) or (Ia), or a pharmaceutically acceptable salt thereof, as claimed in claim 1, 2, 8 or 9 for use as a medicament

15. The use of a compound of formula (I) or (Ia) as claimed in claim 1, 2, 8 or 9, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in the inhibition of a cysteine protease in a warm blooded animal.

16. The use of a compound of formula (I) or (Ia) as claimed in claim 1, 2, 8 or 9, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in the treatment of chronic obstructive pulmonary disease in a warm blooded animal.

17. A method of treating a Cathepsin L or Cathepsin S mediated disease state in mammals which comprises administering to a mammal in need of such treatment an effective

amount of a compound of formula (I) or (Ia) as claimed in claim 1, 2, 8 or 9, or a pharmaceutically acceptable salt thereof.